

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/NL 03/00785

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 G01R33/465

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 G01R

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

INSPEC, WPI Data, PAJ

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>F. GIUBILIEI ET AL.: "Blood cholesterol and MRI activity in first clinical episode suggestive of multiple sclerosis" ACTA NEUROL. SCAND., vol. 106, August 2002 (2002-08), pages 109-112, XP002251481 the whole document</p> <p>—</p> <p>M.N. DEGAONKAR ET AL.: "Sequential proton MRS study of brain metabolite changes monitored during a complete pathological cycle of demyelination and remyelination in a lysophosphatidyl choline (LPC)-induced experimental demyelination lesion model" NMR IN BIOMEDICINE, vol. 15, May 2002 (2002-05), pages 293-300, XP008020901 page 294 -page 299</p> <p>—</p> <p>—</p>	1-3
A		1,3
		—/—



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

- \*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the Invention
- \*X\* document of particular relevance; the claimed Invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed Invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the International search

11 March 2004

Date of mailing of the International search report

18/03/2004

Name and mailing address of the ISA

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PCT/NL 03/00785

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	A.G. DROOGAN ET AL.: "COMPARISON OF MULTIPLE SCLEROSIS CLINICAL SUBGROUPS USING NAVIGATED PSIN ECHO DIFFUSION-WEIGHTED IMAGING" MAGNETIC RESONANCE IMAGING, vol. 17, no. 5, 1999, pages 653-661, XP002251482 page 653 -page 657 -----	1-3
A	WO 98 41882 A (D.L. ARNOLD ET AL.) 24 September 1998 (1998-09-24) page 2, line 25 -page 7, line 33 -----	1
A	US 6 181 134 B1 (L.L. WALD) 30 January 2001 (2001-01-30) column 1, line 32 -column 2, line 34 column 5, line 44 -column 8, line 46 -----	1

**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/NL 03/00785**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 4-15 because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this International application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 4-15

Claims 4 – 15 do not meet the requirements of:

Rule 39.1(iv) PCT – Diagnostic method practised on the human or animal body.

Claims 4, 5 specify:

Gebruik van een biomarker ... voor

- het monitoren van demyelinisatie

- voor diagnose en prognose van multiple sclerose...

The use of a biomarker for monitoring demyelination or for diagnosing / prognosing multiple sclerosis signifies the first step carried out in a diagnostic method, and this step provides the physical data upon necessary for a comparison between normal / abnormal values which comparison results in a final diagnostic. Obviously, the method of claims 4 and 5 is carried out on a human or animal body.

Therefore, claims 4 and 5 do not meet the requirements of Rule 39.1(iv) PCT.

The above arguments apply mutatis mutandis to the subject-matter of claim 6 and of claim 7, dependent upon claim 6; hence, also claims 6 and 7 do not meet the requirements of Rule 39.1(iv) PCT.

Claim 8 specifies:

- verschilprofiel voor de detectie van demyelinisatie in een zoogdier...  
Hence, claim 8 specifies a method of treating NMR spectra, which have been obtained by in vivo NMR spectroscopy, i.e. a method of comparing NMR spectra which comparison step is necessary for arriving at the conclusion that demyelination is present or present to a certain degree, i.e. for establishing a diagnosis practised on the human or animal body.

Therefore, also claim 8 and claims 9 – 11, dependent upon claim 8 do not meet the requirements of Rule 39.1(iv) PCT.

Claim 12 specifies:

- werkwijze voor de detectie van demyelinisatie in een zoogdier...

Hence, claim 12 specifies a diagnostic method 'detectie van demyelinisatie' practised on the human or animal body.

Therefore, also claim 12 and claims 13 and 14, – dependent upon claim 12 –, do not meet the requirements of Rule 39.1(iv) PCT.

Claim 15 specifies:

- werkwijze voor het vervardigen van een verschilprofiel voor demylinisatie in een zoogdier...

...  
- het detecteren van verschillen tussen de genormaliseerde waarden van genoemde eerste en tweede set, ter verkrijgen van genoemd verschilprofiel.

The step of establishing a profile of differences for demyelination in a mammal and the step of detecting differences between a data set of a

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

mammal in good health and a date set of a second mammal is a diagnostic step upon which establishes the conclusion: that demyelination is present or not in the mammal being examined, or that demyelination is present to a given degree 'more or less serious!', is based. Therefore, claim 15 specifies a diagnostic method practised on the human or animal body 'in vivo NMR spectroscopy!', and it does not meet the requirements of Rule 39.1(iv) PCT.

The subject-matter of claims 4 – 15 has not been searched and will not be further examined.

## INTERNATIONAL SEARCH REPORT

Application No  
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Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 9841882	A 24-09-1998	CA CA WO	2200045 A1 2254952 A1 9841882 A1	14-09-1998 24-09-1998 24-09-1998
US 6181134	B1 30-01-2001	US	2001003423 A1	14-06-2001